Cell biology - Two pores better than one?

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are in some way coupled to each other, leading to the formation of — sometimes beautiful — patterns in space and time.

So can synchrony be observed in systems that behave chaotically? One of the hallmarks of chaotic systems that are isolated from one another is that their evolution diverges exponentially fast, even when their initial conditions are very similar. This is why predicting the weather more than a few days in advance is so hard. Therefore, the finding a couple of decades ago that suitably coupled chaotic systems could (under certain conditions) do exactly the opposite, and converge from distant initial conditions to synchronize their chaotic motions, came as a huge surprise[3,4].

The subsequent discovery that lasers can emit light in patterns that are chaotic in time and space clearly implied that remote lasers should be able to synchronize if they receive light from one another, whether through space or through an optical fibre. Experiments soon confirmed this, and with the exchange of only small amounts of light, too[5,6]. The synchronization is sufficiently robust for information to be exchanged: if one of the chaotic laser systems, the transmitter, is perturbed by a message source, it can 'fold' that information into its own chaotic waveform, which it transmits to the input of the second laser system, the receiver. Meanwhile, the receiver's output is a synchronized replica of the transmitter's original, unperturbed chaotic waveform — so the receiver recovers the message as the difference between its input and output waveforms. (Analogously, a radio receiver that is tuned to a carrier frequency recovers information from perturbations of the amplitude or frequency of a periodic waveform.)

Argyris and colleagues[1] take a large stride towards showing that the method of transmitting and receiving information using chaotic waveforms can also work in the real world, without the stable conditions of the laboratory. Applying chaotic systems in real-world communications is a beguiling prospect, because a third party intercepting the signal would have difficulty extracting the information sent. Such security aspects of chaos-based communications admittedly need much further analysis. But as the authors point out, chaotic carrier waveforms offer privacy in a manner that could be complementary to and compatible with conventional software-based and quantum-cryptographic systems.

The remarkable features of the authors' work are the simplicity of their set-up — they use chaotic diode laser systems and instrumentation that are widely available off the peg — and their demonstration that information can be recovered with quite reasonable bit-error rates over a commercial fibre-optic link. The optical fibre used for the experiments in Athens was temporarily free of network traffic, but was still installed and connected to the switches of the network nodes. The authors measured the characteristics of the fibre, such as its attenuation and chromatic dispersion, before the experiment. This allowed them, for example, to exactly counter the effects of dispersion by inserting an appropriate length of dispersion-compensating fibre at the beginning of the link. Three amplifiers were used, one at the transmitter, one 50 kilometres from the transmitter, and one at the receiver, followed by optical filters with bandwidths of around 1 nanometre — this respectively compensated for optical losses and removed spontaneous noise.

The scheme used by Argyris *et al.* exploited time-delayed feedback to generate high-dimensional, high-capacity chaotic waveforms at high bandwidths. This has turned out to be a most fruitful approach: the bit-rate limit of several gigabits in these experiments is set by the electronic and optical components used, and could become much higher with suitably designed systems. For instance, the authors' strategy is compatible with a technique known as wavelength multiplexing; this allows much higher bit rates to pass through a single fibre by transmitting light of many different wavelengths simultaneously.

The exciting possibilities revealed by these experiments[1] may be pursued in other directions that more fully exploit the possibilities available for communication using electromagnetic waves. The vector properties of light waves (their polarization) could be used to encode data[7]. Optical patterns that are chaotic in time and space might also be used to communicate holographic information[8] by generalized synchronization. Here, transmitter and receiver do not share identical synchronized dynamics; instead, the relationship between the two is given by a mathematical function, supplying an additional element of privacy.

The success of such developments will ultimately depend on our willingness to implement new ways of transporting optical signals, as well as on novel transmitters and receivers. The rewards could be considerable, not only in understanding the communication of information using chaotic physical systems. Such work could in the long term also help us to elucidate the workings of that most private of communication networks — the human brain. ■

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CELL BIOLOGY

Two pores better than one?

Arnold J. M. Driessen

The movement of proteins through a cell's membrane requires a dedicated molecular machine. A glimpse of this apparatus in action shows that it has two channels, and hints at how these pores might be regulated.

A cell's membrane bristles with proteins that sense and communicate with its environment, and the cell secretes other proteins to send messages farther afield. To reach their destination, these proteins must travel from the aqueous environment of the cytoplasm where they are synthesized, through the seemingly impenetrable boundary of the lipid membrane. To ease the proteins' emigration, cells use a specialized protein complex called a translocase to direct proteins across or into the membrane. On page 318 of this issue, Mitra *et al.*[1] report the structure of this remarkable complex caught in the act of inserting a newly synthesized protein into the membrane.

Proteins that must be secreted or inserted in the cell membrane are synthesized (translated) by membrane-bound organelles called ribosomes; they have a short sequence at one end (the amino terminus) that acts as an address label to signal their final destination. The translocase consists of a protein-conducting channel (PCC) in the membrane that binds to the ribosome and passes newly synthesized proteins bearing the appropriate address label across or into the cell membrane. The translocase must provide an aqueous path across the membrane for hydrophilic protein segments, as well as a side opening to the membrane lipid phase to release hydrophobic protein segments into the membrane. The aqueous path must be tightly controlled, or valuable ions and molecules will leak out of the cell.

Mitra *et al.*[1] have used cryo-electron microscopy to determine the structure of the Sec translocase, from the bacterium *Escherichia coli*[2], that is associated with a ribosome in the process of synthesizing a protein called FtsQ. They reveal a unique strategy by which a translating ribosome assembles a PCC

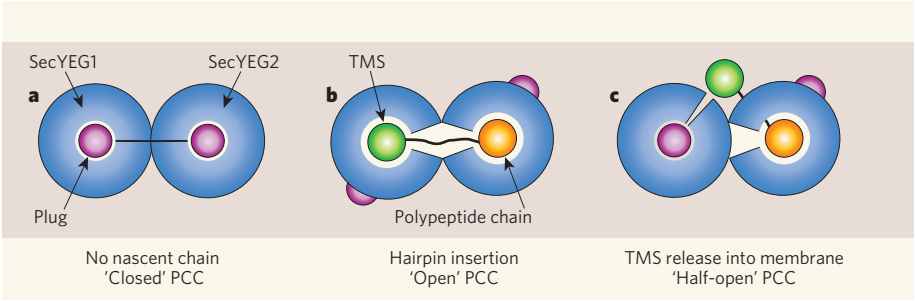

Figure 1 | Initial stages of the translocase mechanism, a model proposed by Mitra *et al.*[1]. The protein-conducting channel (PCC) is shown as though looking through the pore from the inside of the cell. The membrane lipid is shown in light brown. The two SecYEG complexes of the PCC are shown as two clam-shell structures. The ribosome is not shown. **a**, In the 'closed' PCC structure, the channels are sealed by plug domains (purple). **b**, Insertion of a hairpin loop of nascent FtsQ protein with a transmembrane segment (TMS; green) and a hydrophilic segment (orange) will wedge open the SecY clam shells and displace the plugs to open a consolidated pore ('open' PCC). **c**, The ribosome rearranges the PCC, whereupon the inserted TMS is released sideways into the bulk lipid phase of the membrane from the SecYEG1 pore, which then closes. The SecYEG2 pore will remain open, but the channel will be sealed from the lipid phase by a wall formed by SecYEG1. The schematics of the closed and half-open PCC are based on the cryo-electron-microscopic structures described by Mitra *et al.*[1]. The open PCC is hypothetical.

consisting of two separate pores that have different lipid accessibilities.

The Sec PCC is a complex of three proteins — SecY, SecE and SecG — each made of several transmembrane segments[2]. Fully translated, partially folded polypeptide chains of the synthesized protein are pushed or pulled through the translocase channel with the aid of motor proteins — SecA in the case of the Sec translocase. But the translocase can also pass one end of a partially translated 'nascent' protein through, with the ribosome still at work at the other end churning out the growing peptide chain.

A previous structure[3] of a closely related bacterial translocase from *Methanococcus jannaschii* shows that, when it is inactive, SecY resembles a clam shell, with each half of the clam consisting of five transmembrane segments. The SecY halves encompass a funnel-like cavity across the membrane that is blocked by a loop that forms a 'plug' at the external face. Biochemical evidence suggests that polypeptides travel through the centre of SecY[4], and that during this time the plug is displaced[5]. On the inside face of this translocase, large loops extend out of the membrane plane, creating a docking site for the ribosome[6].

On the basis of this structure, it was proposed that the active PCC consists of just one SecYEG complex, and that binding of the protein's address signal would displace the plug and force open the SecY halves to make a channel. However, several observations remained unexplained. For instance, if a single copy of the complex forms the PCC, why have several copies clumped together[7,8] been observed biochemically and structurally? So Mitra *et al.*[1] reasoned that a snapshot of the PCC structure associated with a translating ribosome might provide a better insight. After some nifty experimental trickery to create a stable complex, they managed to catch the translocase red-handed, picturing the ribosome, the peptide chain it was making and the PCC as one complex in unprecedented detail.

Strikingly, Mitra *et al.*[1] found that the ribosome–peptide–PCC structure contains two copies of the SecYEG complex. Computer modelling[9] implied that the two SecYEG complexes face each other, with their lateral gates — the clam-shell mouths — touching (Fig. 1). This is in contrast to a recently proposed back-to-back arrangement[2,8], deduced from a structure obtained in the absence of any other proteins. However, several lines of evidence[5,10] indicate that the back-to-back orientation of the PCC is probably an inactive, and possibly a resting, state of the translocase. The ribosome, and perhaps the SecA motor, might then help to ready the PCC for action by rearranging the individual SecYEGs into the face-to-face orientation.

Mitra and colleagues' structure shows three connections between the internal face of the PCC and the large subunit of the ribosome, including two that contact the large loops of the two SecY proteins — so the ribosome is in the ideal position to direct the rearrangement of the PCC. The structure exhibits a large frontal opening (about 20×40 Å) through which the nascent peptide chain and the connections are accessible from the cytoplasm. Remarkably, each SecYEG complex retains its own separate channel, rather than joining up to make one big one. Moreover, the two channels have different architectures: one is accessible to lipids, so it would seem to be adapted for integrating nascent membrane proteins into the membrane; the other is inaccessible to lipids, making it suitable for the transport of hydrophilic regions of the nascent polypeptide chain.

This latter 'aqueous' pore is occupied by a rod-like shape that seems to correspond to the hydrophilic segment of FtsQ. The structural interpretation suggests that the hydrophobic transmembrane segment of FtsQ is in the lipid phase near the side gate of the other SecY. Mitra *et al.*[1] propose that this might be the site where SecY interacts with other proteins (such as YidC) that could chaperone the transmembrane segments into the membrane. The atomic model also predicts the position of the plug domain that closes the individual pores. In the 'aqueous' SecY channel, the plug appears in its open-state position at the periphery of SecY; but in the other channel, the plug seems to block the exit to the outside of the cell.

Nascent proteins destined for the membrane insert into the PCC as a hairpin, but how this occurs is still speculation. In the cryo-electron microscopy structure, the hairpin of the nascent chain has already slotted into the PCC, so it can provide few answers. Clearly, at some stage a single consolidated pore needs to form to direct the hydrophobic signal sequence or transmembrane segment through the lateral gate into the membrane (Fig. 1b), requiring opening of the 'mouths' of both SecYEG complexes. Once the hairpin has been inserted, the structure might then close up to generate the separate channels. The consolidation and division of the pore are probably controlled by the ribosome, but the mechanistic details remain to be elucidated. Likewise, the PCC structure suggests that the diameter of the consolidated pore may be varied to modify how far the SecYEG mouths open. If a transmembrane segment of the nascent chain is indeed reoriented in the PCC, a consolidated pore would provide sufficient manoeuvring space. Such a pore would also be wide enough to allow partially folded polypeptides through.

Mitra *et al.* present the first snapshot of a translocase in action, taking a significant step towards understanding the highly dynamic organization of this remarkable machine and how it controls distinct functions such as protein translocation and membrane-protein insertion. We eagerly await further developments in elucidating how the PCC is controlled by the motor protein SecA[11], which replaces the ribosome to push fully formed peptide chains through the membrane. ■

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